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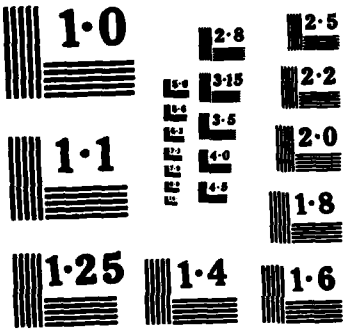

FINAL REPORT: STATISTICAL RESEARCH ON PROBLEMS OF BIODYNAMICS

by

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Dennis E. Smith

— STATISTICS —

— OPERATIONS RESEARCH —

— MATHEMATICS —

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Applied Research in Statistics - Mathematics - Operations Research

FINAL REPORT: STATISTICAL RESEARCH ON PROBLEMS OF BIODYNAMICS

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Kevin C. Burns
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TECHNICAL REPORT NO. 112-19

July 1985

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I. INTRODUCTION

This final technical report prepared under Contract No. N00014-79-C-0128 summarizes a research investigation conducted by Desmatics, Inc. under sponsorship of the Office of Naval Research. This research has focused on problems of biodynamics applicable to the Navy's program at the Naval Biodynamics Laboratory (NBDL). The following sections briefly summarize the research accomplished under this contract and provide a reference list of all technical reports (with abstracts), journal articles, and presentations resulting from this research effort.

II. RESEARCH SUMMARY

The statistical research conducted by Desmatics, Inc. under this contract focused on two major problem areas within the Navy's biodynamics program at NBDL. Those were: (1) impact acceleration injury and (2) ship motion sickness. Additional research was conducted in the area of performance testing, which is relevant to both of the primary research topics. The following three sections provide a brief summary of Desmatics' work in each area.

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A. IMPACT ACCELERATION INJURY

Desmatics research in this area was directed toward the establishment of tolerance limits to $-G_x$ acceleration. This required the development of probabilistic models for impact acceleration injury and Desmatics chose the logistic response model as the generic form most appropriate for that purpose. A major portion of the Desmatics research effort was devoted to the development of optimal procedures for these models. A parallel line of research involved fitting specific response functions to empirical data gathered from $-G_x$ acceleration experiments carried out at NBDL using rhesus monkeys as subjects.

One of the Desmatics technical reports in this area discussed optimal designs for estimation of the parameters of a logistic function. Further research considered the problem of augmenting an existing experimental design. In addition, Desmatics studied procedures for incor-

porating various sources of auxiliary information into the modeling process and thereby improving the parameter estimates. Computational aspects of these procedures were discussed and simulation used to evaluate their efficacy.

Using the NBDL data base consisting of 93 $-G_x$ accelerator runs on rhesus monkeys, several different logistic models were constructed and evaluated. Those models were based on different sets of predictor variables, including the forces and torques in the region of injury, sled profile variables, head dynamic response variables, and the initial position of the head. These models were thoroughly documented and evaluations were made of each variable's ability to predict injury. Additional research involved the extraction of optimal predictor variables from the head dynamic response time traces. In addition, the NBDL rhesus experiments were compared to earlier research on baboons.

As part of its research effort on impact acceleration injury prevention, NBDL conducted a series of experiments designed to test the neurophysiological effects of indirect or inertial head-neck impact acceleration. In these experiments, unanesthetized Rhesus monkeys were subjected to sled accelerations in the -X direction and somatosensory evoked potentials (EPs) were recorded prior, during, and subsequent to impact. A primary objective of these experiments was to determine the extent to which impact produced shifts in latency of various peaks of the (cervical) evoked potentials. Shifts in latency of each peak were plotted as a function of time over the experiment, relative to impact.

Desmatics developed an alternative computational procedure for fitting an exponential model directly to the empirical latency data. In addition, a corresponding FORTRAN program, implementing the computational method, was developed.

Desmatics is currently conducting research on the problem of scaling the experimental results of the $-G_x$ rhesus runs to other species. This research is focused primarily on determining what information is needed for the development of a statistical scaling model and how to obtain that information as efficiently as possible. Such a model would not describe the mechanisms responsible for injury but, by virtue of being based primarily on observed data, would provide predictions which did not depend to a great extent on theoretical assumptions about the mechanical structure and dynamics of the head and neck.

The primary objective of the NBDL research effort is to develop a human injury prediction model. In a previous Desmatics technical report [4], a methodology was outlined for constructing such a model based on injury data for subhuman primates and preinjury data for both subhuman primates and humans. As stated in that report, the methodology requires injury data for at least two species of subhuman primates in order to construct a statistical injury prediction model for humans.

The statistical injury prediction models developed by Desmatics have been based on logistic functions depending on linear combinations of the sled profiles, head dynamic responses, or forces and torques in the region of injury. The forces and torques are intuitively the best variables upon which to base a statistical scaling model. The simplest such model would use the same basic linear combinations multiplied by

a scaling factor for each of the species being considered. The choice of a scaling factor, however, must depend on the injury mechanism.

Examination of the literature in this area has shown that relatively little information is available on the scaling of experimental results to different species. Ommaya and his coworkers [3], following Holbourne [1], have postulated a scaling relation where the ratio of the angular accelerations needed to cause concussion varies inversely with the two-thirds power of the ratio of the body masses. This relation is based on the assumption that relative angular motion between the brain and the skull causes large shear stresses in the brain leading to tissue damage and concussion. However, none of the rhesus experiments run at NBDL resulted in concussion, even though the sled accelerations covered the entire range from very low to lethal levels. Clearly, a different injury mechanism is involved than that which produced concussion in Ommaya's experiments.

Linear acceleration of the head has been shown to produce large pressure gradients and stress waves in the brain [6]. For a given acceleration, the peak pressures are roughly proportional to the length of the skull along the acceleration axis. Therefore, that length may be used to scale between species. However, in the NBDL experiments, no evidence was reported of the cavitation injuries associated with these pressures.

The dynamic response variable which Desmatics found to be the best predictor of fatality in $-G_x$ rhesus runs was the linear acceleration of the head center of gravity in the anatomical +Z direction [5].

Force in this direction stretches the spinal cord and puts stress on the ligaments connecting C1 to the head and C1 to C2. Sufficient force produces ligament failure and subsequent head rotation causes transection of the spinal cord.

Assuming that the neck ligaments in different primates have about the same resistance to stress, failure would occur at equal stress levels for each species. For a given head acceleration, stress is proportional to the head mass and inversely proportional to the cross-sectional area of the ligaments bearing the load at any given point in time. A rough approximation of this last factor might be the average cross-sectional area of the neck for each species.

Future $-G_x$ acceleration experiments are planned at NBDL using chimpanzees as subjects. The approximations given above, though rough, should give some idea of the head acceleration levels needed to produce fatal injuries in this species. However, in order to produce these head accelerations, it is necessary to know how the head dynamic response depends on the sled profile and initial head conditions for each species. This is a problem that could better be solved through a biodynamic modelling approach, rather than a statistical approach.

Desmatics has done extensive research on the design of experiments for the development of logistic injury prediction models. The optimal designs depend on the parameters of the prediction function. Since these parameters cannot be known prior to experimentation, it is best to use a sequential design, where each phase of experimentation depends on the results obtained in previous phases. Desmatics

Technical Report No. 112-5 [2] discusses optimal augmentation of designs for the estimation of the parameters of a logistic function. The procedures discussed in that report may be used to design an efficient sequential experiment for obtaining an injury prediction model for chimpanzees. This model, in conjunction with that for rhesus monkeys, may be used to obtain an empirical scaling factor. This, in turn, may be used in conjunction with the previously mentioned methodology to extrapolate to a statistical injury prediction model for humans.

B. SHIP MOTION SICKNESS

A major component of the Navy's ship motion research program has been the study of single and mixed frequency vertical whole-body sinusoidal motion. Desmatics considered several alternative characterizations of sinusoidal motion and attempted to extend those characterizations to dual-frequency motion. No characterization consistently provided accurate predictions of motion sickness incidence.

Desmatics examined the distributional properties of some existing time to first emesis data. Based on its analysis, Desmatics postulated a mixture of two statistical populations as an overall model of time to first emesis. Empirical evidence suggested that the subpopulation of susceptible volunteers was well-modeled by a Weibull distribution. Further research involved comparing the results of experiments using dual-frequency sinusoidal motion.

C. PERFORMANCE TESTING

Part of the research work at NBDL involves the administration of performance tests in order to evaluate the effects of various factors on performance. Often, each individual is required to take multiple administrations of each of several tests. Desmatics developed a computer program designed to produce a feasible schedule for test administration.

When an individual is tested repeatedly over time, correlations between the scores make statistical analysis difficult. Desmatics chose a model which adequately describes many situations of this type and studied inference procedures for that model. Several candidate test statistics were evaluated with simulated data. Charts and tables were prepared from the simulation results to give bounds for the significance levels of each test statistic.

III. DESMATICS TECHNICAL REPORTS

Desmatics Report Number: 112-1 Date: July 1979

DTIC Number: AD-A071625

Title: AN EXAMINATION OF STATISTICAL IMPACT ACCELERATION INJURY PREDICTION MODELS BASED ON TORQUE AND FORCE VARIABLES

Authors: Dennis E. Smith and John J. Peterson

Abstract: This technical report describes the construction of impact acceleration injury prediction models from a set of twenty-eight $-G_x$ accelerator runs involving Rhesus monkeys with securely restrained torso and unrestrained head. Peak torque and force variables measured during these runs were used to predict injury likelihood. The relative contribution of these variables was examined with respect to the original and a modified version of the data set. Two possible prediction models were used to construct two critical envelopes, i.e., those values of the variables for which the predicted probability of injury (or fatality) is less than or equal to some specified probability. The preferred model was identified and discussed.

Desmatics Report Number: 112-2 Date: August 1979

DTIC Number: AD-A072682

Title: STATISTICAL PROCEDURES FOR EXTRACTING OPTIMAL PREDICTOR VARIABLES FOR USE IN AN IMPACT ACCELERATION INJURY PREDICTION MODEL

Authors: Dennis E. Smith and John J. Peterson

Abstract: An empirical impact acceleration injury prediction model can be based on an underlying logistic function using information extracted from dynamic response data to define independent (predictor) variables. This report describes statistical procedures for the extraction of optimal predictor variables. The application of the statistical techniques of principal components analysis and canonical correlation analysis is described. An outline of how the data analysis may be conducted with the BMDP statistical computer package is discussed.

Desmatics Report Number: 112-3 Date: November 1979

DTIC Number: AD-A077279

Title: SCHEDULER: A COMPUTER PROGRAM FOR SCHEDULING ADMINISTRATION OF PERFORMANCE TESTS

Authors: Robert L. Gardner and Dennis E. Smith

Abstract: This report describes SCHEDULER, a computer program which implements a heuristic scheduling algorithm. This algorithm is designed to produce a feasible schedule for administration of performance tests to a group of subjects who are required to take multiple adminstrations of each of several tests. Provision is made for scheduling up to ten tests in parallel during each of several periods per day. Availability of subjects and tests may be specified in terms of an internal calendar which may be linked to the real-world calendar, so that a completion date for the schedule may be determined. The SCHEDULER program may be used experimentally in evolving scheduling strategies or may be used to produce a working schedule for a real set of circumstances. The results of a series of experimental runs are presented, as well as some conclusions regarding strategies for a specific application. The program input and output formats are described in detail and a system flow chart is provided.

Desmatics Report Number: 112-4 Date: January 1980

DTIC Number: AD-A080572

Title: OPTIMAL DESIGNS FOR ESTIMATION OF THE TWO-PARAMETER LOGISTIC FUNCTION

Authors: Leslie A. Kalish and Dennis E. Smith

Abstract: In this report, optimal designs for weighted least squares and maximum likelihood estimation of the two-parameter logistic function are constructed. In particular, four criteria for optimality are considered: D, A, E and G-optimality. The D and G-optimality criteria are found to be invariant to changes in scale while the A and E-optimality criteria are not. Practical problems which arise in the implementation of the optimal designs are discussed.

Desmatics Report Number: 112-5 Date: May 1980

DTIC Number: AD-A085004

Title: OPTIMAL AUGMENTATION OF EXPERIMENTAL DESIGNS FOR ESTIMATION OF THE LOGISTIC FUNCTION

Authors: Leslie A. Kalish and Dennis E. Smith

Abstract: A criterion for optimal augmentation of an experimental design is applied to the problem of estimating the logistic function. A simulation study is conducted to evaluate the procedure in the two-parameter case. Examples in the development of impact acceleration injury prediction models are given.

Desmatics Report Number: 112-6 Date: August 1980

DTIC Number: AD-A087810

Title: A GENERAL STATISTICAL APPROACH FOR USING AUXILIARY INFORMATION IN THE DEVELOPMENT OF AN IMPACT ACCELERATION INJURY PREDICTION MODEL

Authors: John J. Peterson and Dennis E. Smith

Abstract: This report discusses general procedures for simultaneously incorporating various sources of auxiliary information into an impact acceleration injury prediction model. The sources of auxiliary information considered are supplemental continuous empirical data and a priori knowledge in the form of model parameter estimates and constraints.

Desmatics Report Number: 112-7 Date: February 1981

DTIC Number: AD-A095299

Title: COMPUTATIONAL ASPECTS OF INCORPORATING AUXILIARY INFORMATION INTO AN IMPACT ACCELERATION INJURY PREDICTION MODEL

Authors: John J. Peterson and Dennis E. Smith

Abstract: Auxiliary information may sometimes be used in development of a mathematical model in order to improve the estimated values of unknown parameters. This report discusses computational procedures which allow the application of commonly used nonlinear estimation programs to incorporate various sources of auxiliary information into an impact acceleration injury prediction model.

Desmatics Report Number: 112-8 Date: February 1981

DTIC Number: AD-A096750

Title: PRELIMINARY ANALYSIS OF MOTION SICKNESS INCIDENCE DATA

Authors: Carl A. Mauro and Dennis E. Smith

Abstract: This report analyzes motion sickness data obtained from experiments involving the Office of Naval Research motion generator. Based on the analysis, a mixture of two statistical populations has been postulated as an overall model of time to first emesis.

Desmatics Report Number: 112-9 Date: September 1981

DTIC Number: AD-A105463

Title: A MONTE CARLO STUDY OF THE USE OF AUXILIARY INFORMATION IN THE DEVELOPMENT OF AN IMPACT ACCELERATION INJURY PREDICTION MODEL

Authors: Dennis E. Smith and John J. Peterson

Abstract: This report describes a small-scale Monte Carlo investigation of procedures for incorporating various sources of auxiliary information into an impact acceleration injury prediction model. Parameter estimates are tabulated and compared for standard and modified models. Based on the results of the investigation, the procedures appear to be helpful in reducing the mean square error of predictions.

Desmatics Report Number: 112-10 Date: November 1981

DTIC Number: AD-A107996

Title: ACCELERATION MEASURES AND MOTION SICKNESS INCIDENCE

Authors: Carl A. Mauro and Dennis E. Smith

Abstract: An important aspect of motion sickness research is to establish quantitative relationships between sickness incidence and various parameters of the motions that induce sickness. At present, however, only whole-body vertical sinusoidal motion has been studied to any reasonable degree. The purpose of this report is to examine the predictive utility of six different characterizations of sinusoidal motion and to investigate their possible extension to dual frequency motion.

Desmatics Report Number: 112-11 Date: June 1982

DTIC Number: AD-A116440

Title: RESEARCH ON THE DEVELOPMENT OF A STATISTICAL IMPACT ACCELERATION INJURY PREDICTION MODEL FROM $-G_x$ ACCELERATOR RUNS

Authors: Dennis E. Smith and David Aarons

Abstract: Statistical impact acceleration injury prediction models are developed for the head/neck segment from data obtained during 68 $-G_x$ accelerator runs. These runs involved sub-human primates (Rhesus monkeys) with securely restrained torso and unrestrained head. The data was collected by the Naval Biodynamics Laboratory (NBDL) as part of its research effort on acceleration impact injury prevention. Three classes of prediction models are constructed, one based on sled profile variables, another based on head dynamic response variables only, and the third comprised of the combined set of independent variables. The model predictions are compared with the observed results to evaluate performance.

Desmatics Report Number: 112-12 Date: February 1983

DTIC Number: AD-A125779

Title: THE EFFECT OF ENVIRONMENTAL CHANGE IN SINGLE-SUBJECT EXPERIMENTS

Authors: Kevin C. Burns and Dennis E. Smith

Abstract: Statistical procedures for testing the mean of a first-order autoregressive model are evaluated. Two types of test statistic are considered. One involves estimating the autocorrelation and using that estimate to transform the data. The second type of test statistic is of the form T/w, where w is a function of the estimated autocorrelation and $T = \sqrt{n}\bar{Y}/s$. The usual estimation of the autocorrelation is used initially and compared to a revised estimator which provides less biased estimates. Each procedure is evaluated according to its performance on a set of simulated data.

Desmatics Report Number: 112-13 Date: May 1983

DTIC Number: AD-A129353

Title: STATISTICAL IMPACT ACCELERATION INJURY PREDICTION MODELS BASED ON $-G_x$ ACCELERATOR DATA AND INITIAL HEAD CONDITIONS

Authors: Kevin C. Burns and Dennis E. Smith

Abstract: Statistical impact acceleration injury prediction models are developed using data from 23 high-level $-G_x$ acceleration runs. These runs involve Rhesus monkeys with securely restrained torsos and unrestrained heads. The models are based on peak sled acceleration and initial head conditions. The model predictions are compared with those given in an earlier report based on different data and an estimate of Fisher's information matrix is used to evaluate the relative worth of the two data bases.

Desmatics Report Number: 112-14 Date: May 1983

DTIC Number: AD-A129082

Title: AN EMPIRICAL INVESTIGATION OF SEVERAL TESTS FOR THE MEAN OF A FIRST-ORDER AUTOREGRESSIVE PROCESS

Authors: Kevin C. Burns and Dennis E. Smith

Abstract: Four test statistics are considered for testing hypotheses about the mean of an AR(1) process. Simulated data are used to estimate the actual significance levels obtained when using $t_\alpha(n-1)$ as the critical value. Smoothing functions are fit to the empirical significance levels as functions of sample sizes. These functions are presented graphically and an example given as to how they might be used.

Desmatics Report Number: 112-15 Date: August 1983

DTIC Number: AD-A131930

Title: MOTION SICKNESS INCIDENCE: DISTRIBUTION OF TIME TO FIRST EMESIS AND COMPARISON OF SOME COMPLEX MOTION CONDITIONS

Author: Kevin C. Burns

Abstract: A statistical mixture model is used to fit time-to-emesis data. The Weibull probability distribution is shown to provide a good fit for those subjects who either become sick or withdraw from the experiment within two hours. The second part of the mixture accounts for those subjects who neither quit nor vomit within two hours. The lognormal probability model is shown to give a poorer fit to the data and figures showing the relative fits of the estimated Weibull and lognormal distributions are provided. A nonparametric test is used to compare the five motion conditions of the Correlation Study. That test shows that there are significance differences in severity among the conditions.

Desmatics Report Number: 112-16 Date: May 1984

Title: COMPARISON OF RHESUS MONKEY AND BABOON $-G_x$ EXPERIMENTS

Author: Kevin C. Burns

Abstract: NBDL $-G_x$ acceleration rhesus experiments are compared to the results of Clarke et al. with baboons using the Air Force shoulder harness-lap belt restraint. Baboons are shown to have significantly less tolerance to $-G_x$ acceleration. The differential effect of peak sled acceleration is shown to be the same for each species. The statistical models used are logistic response functions of peak sled acceleration and the initial yaw angle of the head.

Desmatics Report Number: 112-17 Date: May 1984

DTIC Number: AD-A141845

Title: FINAL REPORT: STATISTICAL RESEARCH APPLICABLE TO THE NAVY'S BIODYNAMICS PROGRAM

Authors: Kevin C. Burns and Dennis E. Smith

Abstract: This final technical report prepared under Contract No. N00014-79-C-0128 summarizes a research investigation conducted by Desmatics, Inc. under sponsorship of the Office of Naval Research. This research has focused on problems of biodynamics applicable to the Navy's program at NBDL. The major problem areas studied were impact acceleration injury and ship motion sickness. (Note: This report was submitted as a final contract deliverable. However, subsequent to its submission, the contract was extended.)

Desmatics Report Number: 112-18 Date: June 1985

DTIC Number: Not yet assigned

Title: A NONLINEAR REGRESSION PROCEDURE FOR EVOKED POTENTIAL DATA ANALYSIS

Author: Carl A. Mauro

Abstract: The recording and subsequent analysis of evoked potential activity has proven useful for the evaluation of neural dysfunction resulting from impact acceleration injury involving the head and neck. In animal impact acceleration experiments involving Rhesus monkeys, somatosensory evoked potentials showed an increase in latency following nonlethal experiments. In order to assess quantitatively and objectively the amplitude and duration of the latency effect following impact acceleration, a nonlinear mathematical model has been proposed. This technical report describes a nonlinear regression procedure for fitting the proposed model directly to empirical latency data. A FORTRAN computer program listing is provided.

IV. JOURNAL ARTICLES AND PRESENTATIONS

In addition to the technical reports listed in Section III, significant research findings have been documented in four journal articles. Research accomplishments have also been presented at two scientific and technical meetings. A complete listing of journal publications and technical presentations prepared under this contract is given below:

A. JOURNAL PUBLICATIONS

PREDICTIVE MODEL OF DYNAMIC RESPONSE OF THE HUMAN HEAD/NECK SYSTEM TO $-G_x$ IMPACT ACCELERATION by Dennis E. Smith and W. R. Anderson, Aviation, Space and Environmental Medicine, Vol. 49, pp. 224-233, Jan. 1978.

A STATISTICAL EXAMINATION OF THREE APPROACHES FOR PREDICTING MOTION SICKNESS INCIDENCE by Dennis E. Smith, Aviation, Space and Environmental Medicine, Vol. 53, pp. 162-165, Feb. 1982.

A STATISTICAL ANALYSIS OF MOTION SICKNESS INCIDENCE DATA by Carl A. Mauro and Dennis E. Smith, Aviation, Space and Environmental Medicine, Vol. 54, pp. 253-257, May 1983.

MOTION SICKNESS INCIDENCE: DISTRIBUTION OF TIME TO FIRST EMESIS AND COMPARISON OF SOME COMPLEX MOTION CONDITIONS by Kevin C. Burns, Aviation, Space and Environmental Medicine, Vol. 55, pp. 521-527, June 1984.

B. TECHNICAL PRESENTATIONS

THE STRUCTURE OF A STATISTICAL MODEL FOR PREDICTING IMPACT ACCELERATION INJURY, The Neuroelectric Society 1977 Annual Meeting, Marco Beach, FL, Dec. 1977.

ACCELERATION MEASURES AND MOTION SICKNESS INCIDENCE, International Workshop on Research Methods in Human Motion and Vibration Studies, New Orleans, Sept. 1981.

V. REFERENCES

[1] Holbourn, A.H.S. (1943). "Mechanisms of Head Injuries," Lancet, Vol. 2, pp. 438-441.

[2] Kalish, L.A. and D.E. Smith (1980). "Optimal Augmentation of Experimental Designs for Estimation of the Logistic Function," Desmatics, Inc. Technical Report No. 112-5.

[3] Ommaya, A.K., A.E. Hirsch, P. Yarnell, and A.E. Harris (1972). "Scaling of Experimental Data on Cerebral Concussion in Sub-Human Primates to Concussion Threshold for Man," Proceedings of the Eleventh Stapp Car Crash Conference, SAE, New York, pp. 47-52.

[4] Smith, D.E. (1976). "Research on Construction of a Statistical Model for Predicting Impact Acceleration Injury," Desmatics, Inc. Technical Report No. 102-2.

[5] Smith, D.E. and D. Aarons (1982). "Research on the Development of a Statistical Impact Acceleration Injury Prediction Model from $-G_x$ Accelerator Runs," Desmatics, Inc. Technical Report No. 112-11.

[6] Unterharnscheidt, F. and K. Sellier (1966). "Mechanisms and Pathomorphology of Closed Brain Injury," Head Injury Conference Proceedings, J.B. Lippincott Co., Phila., PA, pp. 321-341.

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Performance Testing
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Mixture Distributions
Autoregressive Process

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

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